pended jointly on the disciplines of molecular biology, cell biology, biochemistry, and physiology. The current focus is to characterize the machinery that drives RNA localization. It will then be important to reconstitute individual transport steps in vitro, e.g., the formation of RNPs, the transport of these granules along the cytoskeleton, and the regulation of translation of localized transcripts. Since it has now been possible to visualize the localization of individual transcripts in the living *Drosophila* oocyte, an important challenge will be to transfer this technology to other leading model systems in order to understand, at the molecular level, how cells regulate mRNA localization in response to various biological stimuli.

Michael Kiebler and Paolo Macchi
Max-Planck-Institute for Developmental Biology
Spemannstrasse 35
D-72076 Tübingen
Germany

Mysteries of Motor Mechanics

Mechanics of Motor Proteins and the Cytoskeleton
By Jonathan Howard
Sunderland, MA: Sinauer Associates, Inc.
367 pp. $59.95

Although he was talking about the art of detection, the following quotation from Sherlock Holmes readily describes many aspects of scientific sleuthing:

Breadth of view is one of the essentials of our profession. The interplay of ideas and the oblique uses of knowledge are often of extraordinary interest.
—Sir Arthur Conan Doyle, *The Valley of Fear*, 1915

Indeed, breadth of view is certainly needed as one scrutinizes the recent explosion of detailed technical reports in the field of cytoskeletal motility. To date, we have many clues but only a few unequivocal answers to central questions. While we know that the majority of motile processes are dependent on the ability of specialized motor proteins to move along cytoskeletal filament systems, we are only starting to understand the details of how motors take their steps, why some motors take multiple steps while others fall off their cytoskeletal substrates after a single step, or the role of the dynamics of the filament systems themselves in providing motile force.

The best-characterized motors are skeletal muscle myosin, an actin-based motor, and conventional kinesin, which transports cargo along microtubules. Both motors convert the energy present in the γ-phosphate bond of ATP into directed motility using a mechanochemical cycle. Early studies with myosin led to the current and prevalent model of motor function, which has two key tenets. First, the motor cycles between two states: attached to and detached from the cytoskeleton. Second, conformation changes occur in the motor during both the attached and unattached states to generate motility in a specific direction along the cytoskeletal filament. Upon the discovery of kinesin and for several years afterward, it was generally thought that kinesin and myosin motors would have different mechanisms of action. These differences were inferred in part by determinations that individual kinesin molecules can take several hundred steps along microtubules without detaching, whereas myosins take a single step along an actin filament before detaching. Surprisingly, the solution of X-ray crystal structures of myosin and kinesin illustrated that the two motors share common core domains involved in converting the energy of ATP hydrolysis to conformational changes. The unexpected similarity between the two molecules gave rise to extensive interplay between the kinesin and myosin groups, as discoveries in one arena were suddenly directly applicable to the other.

A perusal of recent papers shows that the motility field has attracted molecular biologists, biophysicists, and mathematicians to a subject originally populated by physiologists, biochemists, and cell biologists. Much of this development can be seen in the speed with which technologies such as optical laser tweezers and single molecule fluorescence have been embraced. These methodologies have propelled studies that examine the forces generated and distances traveled by individual motor molecules. In conjunction with classic ATPase kinetic analyses of motors, a clearer picture of the details of the mechanochemical cycle is emerging. For example, when optical tweezers are used to generate a load for kinesin to work against, eight nanometer steps corresponding to the periodicity of tubulin dimers in the microtubule lattice are readily seen. Further analyses suggest that two or more substeps are likely to take place during each eight-nanometer step taken by kinesin. The exact details of how this may happen are still murky and several controversial models exist.

What background is required to understand the increasingly elaborate mathematical models of the mechanochemical cycle of cellular motility? As its name suggests, the cycle can be broken into two main components, the chemical and the mechanical. Although the chemical component of cellular motion is similar to other chemical problems described in the biological literature, the same is not true of the mechanical component. *Mechanics of Motor Proteins and the Cytoskeleton* was intended to fill that void by providing an understanding of the mechanics of motility especially for biologists.

Howard's approach in writing *Mechanics* is to reduce concepts to the most basic physical principles and proceed to build the case for a particular point of view or model. The book is divided into three major sections that expand upon each other. The first section, referred to in the Introduction as "Mechanics 101 for biologists" discusses the basic physical principles that are important to small molecules. The concepts in this section are certainly not new; they are based on many of the classic principles of physics. But what is new and refreshing is the continual adaptation and scaling of these principles to the microscopic world of single molecules. The mathematical bias and frequent equations provided do not detract from the conveyance of information, as

the more detailed explanations and proofs are relegated to the appendix. A useful common thread in this section and throughout the entire book is the comparison of the relative strengths of the multitude of forces that act upon small molecules. The first section will go a long way in guiding the less physically or mathematically inclined to a better understanding of principles critical to single molecule processes.

The second section advances beyond hypothetical proteins to the three major cytoskeletal filament systems—actin filaments, microtubules, and intermediate filaments. After concise chapters about the structure and mechanics of the cytoskeleton, the focus of the section is three chapters that discuss the forces and process of polymerization. Unfortunately, the first of these chapters discusses multiple simplistic models of polymerization that ignore the role of nucleotide hydrolysis in polymerization. While this was seemingly done to allow the reader to better appreciate the role of nucleotide hydrolysis discussed later, this approach may make the subject more difficult for those that are not already familiar with current models of dynamic instability.

The heart of *Mechanics* is definitely the five-chapter motor proteins section, where motility models are examined from four distinct points of view: structure, speed, ATP hydrolysis, and step forces of motor proteins. The structural chapter provides a synopsis of several decades of structural studies into the different motor families. As such, it does not provide all the details of structural conformations involved in the mechanochemical cycle, but it illustrates the similarities between kinesin and myosin and provides a good foundation for the following chapters. The next two chapters do a superb job relating the duty cycle of motors (the percentage of time they are bound to the cytoskeleton) to the speed and processivity of motors, and describing the ATP hydrolysis cycle of motors in an intelligent fashion. These concepts are not easy to convey, and Howard's treatment of these subjects is a strength of the book. Examinations of motor step sizes and the forces involved using optical tweezers are among some of the more glamorous experiments in biology, and the chapter describing these experiments both portrays how these experiments are carried out and provides the main conclusions of studies on multiple motors.

The last chapter examines myosin and kinesin motility and attempts to summarize and integrate concepts discussed throughout the book by relating the microscopic single molecule and macroscopic in vivo worlds of motors. Howard's personal model of how two-headed kinesin may move hand-over-hand is presented at the expense of other models that are present in the field. I would have preferred active and in depth discussion of the strengths and weaknesses of multiple models from the mechanical perspective provided throughout the book. For this reason, future readers of the book may want to remember that *Mechanics* does not always relate all sides of the motor story.

Mechanics is not meant to be an all-inclusive tome on motor proteins; it succeeds by focusing specifically on the mechanics of molecules involved in cellular motility. The book is a great launching point for gaining a biophysical understanding of the current detailed literature of motility which is increasingly filled with mathematical models describing motility data. As such, it will benefit students of a wide range of biological and physical backgrounds who are interested in understanding the nuts-and-bolts of cellular motility. The organization and reductionist theme of the book readily lend themselves to discussion of basic physical concepts and principles. In summary, *Mechanics* provides an oblique and refreshing perspective to the motility field that will guide those new to the field to an appreciation of the mechanics of cellular motility.

Stephen J. King[1]
Department of Biology
Johns Hopkins University
Baltimore, Maryland 21218
[1] Present address: Division of Molecular Biology and Biochemistry, School of Biological Sciences, University of Missouri at Kansas City, Kansas City, Missouri 64110.

Endocytosis: Molecules, Membranes, and Movements

Endocytosis
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In transmission electron micrographs, the peripheral cytosol of a typical eukaryotic cell is dominated by a profusion of membrane-bound organelles and small membrane intermediates. Several decades ago, these images, along with emerging subcellular fractionation techniques, led to the birth of the field of intracellular protein trafficking. In time, the internal membrane-bound structures that sparked this line of investigation were characterized, revealing a central tenet of membrane-based protein and lipid movements within the cell: the endoplasmic reticulum–Golgi complex–plasma membrane–endosome–lysosome interrelationship. We know now that the morphological complexity of these static images belies the dynamic nature of membrane traffic within the cell. Lipid and protein flux is relentless and organelle identity is only maintained by complex sorting decisions and precise targeting mechanisms.

Endocytosis is the process of internalization and subsequent sorting of macromolecules from the cell exterior. The endocytic pathway thus shuttles material along specific but varied itineraries between the plasma membrane, endosomes, lysosomes, and the Golgi apparatus. Endosome, of course, does not describe a single, morphologically homogeneous functional organelle, but is rather a blanket term for a malleable and pleiomorphic population of membrane structures charged with overseeing diverse trafficking operations with a high degree of fidelity. Here, form recapitulates function. Shortly after uptake, membrane-bound transport carriers fuse to form early endosomes. These peripherally located early endosomes quickly and efficiently segregate recycling plasma membrane proteins into thin tubular emanations